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## United States Patent [19]

Hallenbeck et al.

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5,998,205

[45] Date of Patent:

Dec. 7, 1999

# [54] VECTORS FOR TISSUE-SPECIFIC REPLICATION

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#### Related U.S. Application Data

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	cation No. 08/348,258, Nov. 28, 1994, abandoned.

[51]	Int. Cl.6	
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[56] References Cited

### U.S. PATENT DOCUMENTS

5,416,017	5/1995	Burton et al	435/325
5,436,146	7/1995	Shenk et al	435/455
5,585,096	12/1996	Martuza et al	424/93.2
5,698,443	12/1997	Henderson et al	. 514/44
5,728,379	3/1998	Martuza et al	424/93.2
5,747,469	5/1998	Roth et al	. 514/44
5,804,407	9/1998	Tamaoki et al	435/69.1

#### FOREIGN PATENT DOCUMENTS

WO95/12660 5/1995 WIPO . WO96/18418 6/1996 WIPO . WO96/34969 11/1996 WIPO .

#### OTHER PUBLICATIONS

Vile et al. (Molecular Medicine Today, vol. 4, 2:84-92, 1998).

Russel (European Journal of Cancer, vol. 30A, 8:1165–1171, Aug. 1994).

Smith et al. (Human Gene Therapy, 5:29-35, 1994).

Abe. M., and Kufe. D., "Characterization of cis-acting elements regulating transcription of the human DF3 breast carcinoma-associated antigen (MUC1) gene," *Proc. Natl. Acad. Sci. USA* 90:282-286 (Jan. 1993).

Grooteclaes, M., et al., "The 6-Kilobase c-erbB2 Promoter Contains Positive and Negative Regulatory Elements Functional in Humn Mammary Cell Lines." Cancer Res., 54:4193-4199 (Aug. 1994).

Kovarik, A., et al., "Analysis of the Tissue-specific Promoter of the MUC1 Gene," J. Biol. Chem. 268:9917-9926 (May 1993).

Max-Audit, L. et al., "Transcriptional Regulation of the Pyruvate Kinase Erythroid-specific Promoter," J. Biol. Chem. 268:5431-5437 (Mar. 1993).

Morishita, K., et al., "A Novel Promoter for Vascular Endothelial Growth Factor Receptor (fit-1) That Confers Endothelial-specific Gene Expression," J. Biol. Chem. 270:27948-27953 (Nov. 1995).

Nakabayashi, H., et al., "A Position-Dependent Silencer Plays a Major Role in Repressing α-Fetoprotein Expression in Human Hepatoma," *Mol. Cell. Biol.* 11:5885-5893 (Dec. 1991).

Pang. S., et al., "Prostate Tissue Specificity of the Prostate-Specific Antigen Promoter Isolated from a Patient with Prostate Cancer," *Human Gene Therapy* 6:1417–1426 (Nov. 1995).

Richards. C.A.. et al., "Transcriptional Regulatory Sequences of Carcinomembryonic Antigen: Identification and Use with Cytosine Deaminase for Tumor-Specific Gene Therapy." Human Gene Therapy 6:881-893 (Jul. 1995). Babiss. L.E. et al., "Cellular Promoters Incorporated inot the

Babiss, L.E. et al., "Cellular Promoters Incorporated into the Adenovirsu Genome: Effect of Viral DNA Replication on Endogenous and Exogenous Gene Transcription." *J. Mol. Biol.* 193:643–650 (1987).

Blaese, R.M. et al., "In Situ Delivery of Suicide Genes for Cancer Treatment," *Eur. J. Cancer* 30A(8):1190–1193 (Aug. 1994).

Brown, D., "Gene Therapy 'Oversold' by Researchers, Journalists." The Washington Post. p. A22. Dec. 8, 1995. Chellappan, S. et al., "Adenovirus E14, simian virus 40 tumor antigen, and human papillomavirus E7 protein share the capacity to disrupt the interaction between transcription factor E2F and the retinoblastoma gene product," *Proc. Natl. Acad. Sci. USA* 89:4549–4553 (1992).

#### (List continued on next page.)

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Attorney, Agent, or Firm—Sterne. Kessler. Goldstein & Fox
P.L.L.C.

#### [57] ABSTRACT

The invention generally relates to targeted gene therapy using recombinant vectors and particularly adenovirus vectors. The invention specifically relates to replication-conditional vectors and methods for using them. Such vectors are able to selectively replicate in a target tissue to provide a therapeutic benefit from the presence of the vector per se or from heterologous gene products expressed from the vector and distributed throughout the tissue. In such vectors, a gene essential for replication is placed under the control of a heterologous tissue-specific transcriptional regulatory sequence. Thus, replication is conditioned on the presence of a factor(s) that induces transcription or the absence of a factor(s) that induces transcription of the gene by means of the transcriptional regulatory sequence with this vector; therefore, a target tissue can be selectively treated.

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